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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/619,144	07/19/2000	Ulrich Mohr	29089/34670A	1600

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EXAMINER	
SANDALS, WILLIAM O	

ART UNIT	PAPER NUMBER
1636	21

DATE MAILED: 10/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/619,144	MOHR ET AL.	
	Examiner	Art Unit	
	William Sandals	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☒ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-27 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-27 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *6-10-2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

Claims 1, 3-27 and 32 are pending.

The rejection of claims 1 and 3-27 under 35 USC 112, first paragraph, written description, has been overcome by amendment to the claims and the rejection is withdrawn.

The rejection of claims 1 and 3-27 under 35 USC 112, second paragraph, has been overcome by amendment to the claims and the rejection is withdrawn.

The rejection of claims 1, 3-27 and 32 under 35 USC 103 has been overcome by amendment to the claims and the rejection is withdrawn.

Claims 1, 3-27 and 32 are rejected under new grounds below. A response to arguments in the Paper filed June 10, 2003, regarding the teachings of US 5,424,209 (Kearney) and JP 402 119772 (Hamazaki) follows the newly made rejection under 35 USC 103(a) below.

Drawings

New formal drawings were received on June 10, 2003. The drawings are approved by the draftsman.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8, 9, 14 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 recites the limitation "a culture medium supply line" in lines 1-2. Claim 8 depends from claim 7, which recites "a common culture medium supply line". It is unclear if the "a culture medium supply line" of claim 8 is intended to be an additional culture medium supply line or the same culture medium supply line as the "a common culture medium supply line" of claim 7. The claim is therefore vague and indefinite.

Claim 14 recites the limitation "the supply mechanism" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

Claim 20 recites the limitation "the outer housing" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3 and 21-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,175,092 (Gabriels, Jr.) in view of JP 402 119772 (Hamazaki, of record).

The claims are drawn to a culturing device comprising a culture container with a removable, porous, horizontal cell culture insert. There is a supply mechanism for introducing the medium to the culture container, and for discharging the medium from the culture container. There is a liquid level sensor for controlling the supply mechanism. A cell culture on the surface of the horizontal cell culture insert may be submerged, or may be in a basal supply condition, such that the surface of the culture is above the level of the liquid medium. The basal condition provides media to the cells by capillary flow of the media from below the level of the cell culture through the porous horizontal cell culture insert. The basal condition allows the cells to be exposed to gases, aerosols and particulates from above. Components of the culturing device may be made of materials, which can withstand sterilization. The materials may be silicone or glass. The supply mechanism may be a bi-directional (peristaltic) pump. There may be a pair of level sensors to control the liquid level in the culture container. There may be a programmable controller which controls the liquid level in a time-dependent manner.

Gabriels, Jr. teaches a cell culturing device comprising a culture container with a porous, removable, horizontal, cell culture insert at the summary (columns 1-2). The cells are grown in a submerged condition, and then the cells are raised above the level of the medium, such that the media is drawn by capillary attraction up through the porous horizontal cell culture insert, allowing the cells to be exposed to gases and aerosols from above (see column 2, lines 43-63). Components of the cell culture device are sterilizable (e.g. glass fibers). The cells of Gabriels, Jr. are taught to be in a

submerged condition and then raised to a level such that the cells are exposed to a gaseous environment. The instant claims and specification do not set a requisite time limit upon the term "sustained", and therefore, a "sustained" condition may be any length of time.

The cells of Gabriels, Jr. are exposed to the gaseous environment of the culture container and would therefore, also be inherently exposed to any aerosols or particulates present in the culture chamber.

Gabriels, Jr. does not teach a system with a level sensor and a supply mechanism for raising and lowering the level of the medium, which may be controlled by a programmable controller in a time-dependent manner.

Hamazaki teaches at pages 2-3 (see item "2. Claim"), an automated cell culturing device comprising a cell culture container. The level of the liquid medium in the culture container is adjusted to submerge the cells and then adjusted to drop below the surface of the cells, which allows the cells to be exposed to aerosols and gases. The cell culturing device has a level sensor for controlling the liquid medium level in the culture container. A supply mechanism responds to signals from the liquid level sensor (forked photoelectric barrier – see pages 12-13), which is controlled by a programmable controller in a time-dependent manner. Hamazaki teaches that the supply mechanism is a pump. Components of the cell culturing device may be silicone or glass (which are sterilizable). Hamazaki teaches at the bottom of page 4, bridging to the top of page 5, that automation of the cell culture device is desirable since the automation optimizes the conditions for cell growth, which are difficult for an operator to control without the

automation. Hamazaki teaches that the cells are alternately submerged and then the level of the tissue culture fluid is lowered to expose the cells to a gaseous environment.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to combine the cell culturing device with a removable, porous, horizontal insert, where the cells are raised above the level of the medium as taught by Gabriels with the automated cell culturing device which raises and lowers the level of the medium above and below the level of the cells in culture as taught by Hamazaki because both Gabriels and Hamazaki teach the desirability of lowering the level of the medium below the level of the cells to expose the cells to a gaseous environment. One of ordinary skill in the art would have been motivated at the time the instant invention was made to combine the cell culturing device with a removable, porous, horizontal insert, where the cells are raised above the level of the medium as taught by Gabriels with the automated cell culturing device which raises and lowers the level of the medium above and below the level of the cells in culture as taught by Hamazaki for the expected benefit of optimizing the culture conditions for cell growth as taught by Hamazaki. Further, one of ordinary skill in the art would have a reasonable expectation of success in combining the teachings of Gabriels, Jr. who demonstrate a cell culturing device with a removable, porous, horizontal insert, where the cells are raised above the level of the medium and Hamazaki who demonstrate an automated cell culturing device which raises and lowers the level of the medium above and below the level of the cells in culture.

Claims 1, 3-15, 19-27 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,175,092 (Gabriels, Jr.) in view of JP 402 119772 (Hamazaki, of record) as applied to claims 1, 3 and 21-27 above, and further in view of US 5,424,209 (Kearney, of record).

The claims are drawn to the invention described above and to the culturing device with a plurality of culture containers. The plurality of culture containers may be associated with a pair of discharge lines, a common culture medium supply line, and a vertically adjustable level sensor, which may be a forked photoelectric barrier. The level sensor may continuously sense the media level, and may contain a level switch. The common culture medium supply line may be connected to a culture medium supply distribution system. The system may have an exterior housing with discrete modules within the housing, such that there is a culture container within each module and ports for connecting to the common culture medium supply line, and discharge lines.

Gabriels, Jr. and Hamazaki teach the culturing device as described above, where Hamazaki teaches a vertically adjustable, forked photoelectric barrier for detecting the level of the media in the culture container (see pages 12-13 of Hamazaki).

Gabriels, Jr. and Hamazaki do not teach a plurality of culture containers, where the plurality of culture containers may be associated with a pair of discharge lines, a common culture medium supply line, nor that the level sensor may continuously sense the media level, and may contain a level switch, nor that the common culture medium supply line may be connected to a culture medium supply distribution system.

Kearney teaches a cell culture and testing system with a sealed exterior housing that contains discrete modules that contain a culture container with microcarriers (removable horizontal cell culture inserts) (see the summary). There is a common medium supply line, with connection ports to each module. There is a common discharge line with connection ports to each module. The fluid is pumped by peristaltic pumps (see the claims). A programmable controller maintains the fluid levels in each container. The modules are heated by an exterior housing which surrounds each module with a peltier heating unit (see the claims). The system may be sterilized (see column 19). Kearney teaches that multiple modules are desirable to perform multiple experiments by exposing the cells to various liquid, solid or gaseous materials (see column 20, lines 32-59). The device allows the performance of rapid, multiple and reproducible studies, also increasing efficiency (see columns 20 and 21).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to combine the cell culturing device with a removable, porous, horizontal insert, where the cells are raised above the level of the medium as taught by Gabriels with the automated cell culturing device which raises and lowers the level of the medium above and below the level of the cells in culture as taught by Hamazaki with the cell culture and testing system with a sealed exterior housing that contains discrete modules that contain a culture container with microcarriers as taught by Kearney because Gabriels, Jr., Hamazaki and Kearney teach a cell culture module for the long term culture of cells. One of ordinary skill in the art would have been motivated at the time the instant invention was made to combine the cell culturing

device with a removable, porous, horizontal insert, where the cells are raised above the level of the medium as taught by Gabriels with the automated cell culturing device which raises and lowers the level of the medium above and below the level of the cells in culture as taught by Hamazaki with the cell culture and testing system with a sealed exterior housing that contains discrete modules that contain a culture container with microcarriers as taught by Kearney for the expected benefit of increasing cell culturing efficiency and for the performance of rapid, multiple and reproducible cell culture experiments and studies. Further, one of ordinary skill in the art would have a reasonable expectation of success in combining the teachings of Gabriels, Jr. who demonstrates a cell culturing device with a removable, porous, horizontal insert, where the cells are raised above the level of the medium with Hamazaki who demonstrates an automated cell culturing device which raises and lowers the level of the medium above and below the level of the cells in culture and with Kearney who demonstrates a cell culture and testing system with a sealed exterior housing that contains discrete modules that contain a culture container with microcarriers.

Claims 1, 3-27 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,175,092 (Gabriels, Jr.) in view of JP 402 119772 (Hamazaki, of record) and further in view of US 5,424,209 (Kearney, of record) as applied to claims 1, 3-15, 19-27 and 32 above, and further in view of US 4,974,952 (Focht).

The claims are drawn to the invention described above and to the heat controlling unit, which has a temperature control medium, which flows through a temperature control housing.

Gabriels, Jr., Hamazaki and Kearney teach the invention as described above. Kearney teaches a peltier heating unit which surrounds the culture container.

Gabriels, Jr., Hamazaki and Kearney do not teach a heat controlling unit which has a temperature control medium, which flows through a temperature control housing.

Focht teaches the use of either a peltier heating unit or a liquid filled heating unit to maintain the temperature of a chamber filled with tissue culture medium and cells. Focht teaches that the peltier heating unit and the liquid filled unit are equivalent for the purposes of maintaining the temperature of cells in a chamber filled with medium.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to use in the alternative a liquid filled heating system as taught by Focht in the cell culturing device with a removable, porous, horizontal insert, where the cells are raised above the level of the medium as taught by Gabriels which is combined with the automated cell culturing device which raises and lowers the level of the medium above and below the level of the cells in culture as taught by Hamazaki and which is combined with the cell culture and testing system with a sealed exterior housing that contains discrete modules that contain a culture container with microcarriers as taught by Kearney because Focht teaches the equivalence of a peltier heating system and a liquid filled heating system to maintain the temperature of cells in a chamber filled with medium. One of ordinary skill in the art would have been motivated

to use a liquid filled heating system in the alternative to a peltier heating system because both systems are well known in the art and absent any evidence to the contrary, it is within the purview of an ordinary skilled artisan to use either means to heat a chamber containing tissue culture medium and cells. Further, one of ordinary skill in the art would have a reasonable expectation of success in combining the teachings of Gabriels, Jr. who demonstrates a cell culturing device with a removable, porous, horizontal insert, where the cells are raised above the level of the medium with Hamazaki who demonstrates an automated cell culturing device which raises and lowers the level of the medium above and below the level of the cells in culture, with Kearney who demonstrates a cell culture and testing system with a sealed exterior housing that contains discrete modules that contain a culture container with microcarriers, and with Focht who demonstrates the alternative, equivalent use of a peltier heating system and a liquid filled heating system.

Response to Arguments

Arguments presented in Paper No. 20, filed on June 10, 2003 at page 8 assert that Hamazaki and Kearney do not teach or suggest a porous surface for culturing, nor a culture insert with a horizontal culture surface, nor a basal culture medium supply condition, nor a system which can achieve both a sustained submerged culture medium supply condition and a sustained basal culture medium supply condition. At page 9, it is conceded that Kearney may teach a horizontal cell culture insert, albeit that the insert is not porous.

Neither Hamazaki nor Kearney are relied upon for teaching porous cell culture inserts, and Hamazaki is silent on the issue of horizontal cell culture surfaces.

Kearney teaches that an insert may be used in the culture modules. The culture surface provided in the culture container of Kearney is shown in the drawings as a horizontal culture surface. Therefore, the insert of Kearney is set upon the horizontal culture surface of the culture container, the result being that the culture surface of the insert is horizontal.

Hamazaki teaches that the liquid levels in the culture container may be set to any desired level. Hamazaki teaches an alternating submerged condition and then lowering the liquid level to expose the surface of the cells in the culture container. Since the instant claims and specification do not provide a requisite length of time for either the sustained submerged condition or the sustained basal supply condition, any length of time may be deemed to fulfill the limitation of "sustained". Therefore, Hamazaki teaches a "sustained" condition, in respect to the length of time that the cells are either submerged or exposed to the gaseous and aerosol environment of the tissue culture container.

The remaining arguments presented in Paper No. 20 do not apply to the newly made rejection above. Therefore, these arguments will not be addressed further.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William Sandals whose telephone number is (703) 305-1982. The examiner can normally be reached on Monday through Thursday, 7:30 – 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

William Sandals

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